

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Patent Application No. 10/806,088

Applicant: Flack et al.

Filed: March 22, 2007

TC/AU: 1614

Examiner: James D. Anderson

Docket No.: 225011 (Client Reference No. E-133-1990/0-US-03)

Customer No.: 45733

APPELLANTS' REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Appellants hereby file a Reply Brief to the Examiner's Answer. The Examiner's answer was mailed by the U.S. Patent and Trademark Office on October 2, 2007, thereby making this Reply Brief due on December 2, 2007. This Reply Brief is provided in further support of the appeal of the decision of the final rejection of claims 8-14, 16, and 38-43, as set forth in the Office Action dated March 19, 2007.

Status of Claims

Claims 8-14, 16, and 38-43 are currently pending and are the subject of this appeal.

Grounds of Rejection to be Reviewed on Appeal

1. Whether claims 8-10, 16, and 38-43 are unpatentable under 35 U.S.C. § 103(a) over Wu (*Cancer Research*, 49: 3754-3758 (1989)) in view of Band (*Gynecologic Oncologists*, 23: 261 (1986)), Zhang (*Acta Academiae Medicinae Sinicae*, 7: 384-387 (1985)), and other relevant prior art.

2. Whether claims 11-14 are unpatentable under 35 U.S.C. § 103(a) over Wu (1989), Band (1986), and Zhang in further view of Wu (*Clin. Pharmacol. Ther.* 39: 613-618 (1986)) and other relevant prior art.

Argument

The Examiner's Answer repeats the rejections and reasoning set forth in the Office Action dated March 19, 2007. Appellants resubmit that the Examiner has erred in determining the scope and content of the prior art and by not considering prior art which taught away from the invention. When viewed as a whole, the prior art would not have led one of ordinary skill in the art to have a reasonable expectation of success in using (-)-gossypol in the treatment of cancer in humans.

In particular, the Examiner's Answer fails to fully consider the teaching of Band (*Gynecologic Oncology*, 32:273-277 (1989)), which is a publication by the same investigators of Band (1986), which was cited during prosecution and relied upon in support of the Examiner's rejections.

As discussed in Applicants' Appeal Brief, Band (1989) describes studies where the activity of the gossypol enantiomers was compared in both cancerous and normal cell lines. In Table 1 on page 276, Band (1989) presents data showing the non-selective activity of (-)-gossypol. In this subsequent and more clinically relevant study than that recited in Band (1986), the same investigators concluded that the anti-proliferative action of gossypol is non-selective with respect to cell type, thereby making it as lethal to normal, non-cancerous, reproductive tract cells as to cancer cells.

The Examiner's Answer seeks to minimize the teaching of Band (1989) by stating an unawareness "of any clinically used anticancer drug that is not toxic to normal, non-cancerous cells to some extent" (Examiner's Answer, p. 8). However, the Examiner's Answer fails to address the fact that the teaching of Band (1989) does not merely indicate that (-)-gossypol is toxic to non-cancerous cells "to some extent." Rather, Band (1989) would have taught one of ordinary skill in the art that (-)-gossypol was so unselective and so toxic as to be unsafe in the treatment of cancer in humans.

Band (1989) reported on the effect of the individual gossypol enantiomers on both cancerous and normal cell lines and concluded that the anti-proliferative action of gossypol and each of its enantiomers is *non-selective*. In other words, (-)-gossypol was found to kill cancerous and non-cancerous cells at the same rate, thereby making (-)-gossypol as lethal to normal, non-cancerous, reproductive tract cells as to the intended cancer cell targets. While anticancer drugs may be lethal to non-cancerous cells in addition to cancerous cells, the key

feature of many anticancer drugs is some measure of selectivity, i.e., that the anticancer drugs will preferentially kill cancer cells over non-cancerous cells. In the absence of such selectivity, or preferential killing of cancer cells as compared to non-cancerous cells, for a particular compound, one of ordinary skill in the art would not reasonably believe that the compound could be useful in the treatment of cancer.

Thus, one of ordinary skill in the art would not have so readily dismissed Band (1989), as is done in the Examiner's Answer, by characterizing Band (1989) as disclosing the "typical" toxicity of anticancer drugs to non-cancerous cells.

In view of the teachings of the non-selective cytotoxicity of gossypol reported in Band (1989), the prior art would not have caused one of ordinary skill in the art to reasonably expect that (-)-gossypol would be an effective treatment of cancer in humans. More specifically, as of the effective filing date for the present application, one of ordinary skill in the art would not have believed that it would have been possible to successfully determine a safe and effective dosage range in genetically heterogenous humans for a drug that displays such a general toxic effect *in vitro* and such a narrow window of efficacy and safety in a genetically homogenous population of in-bred rodents (see Declaration of Dr. Marcus Reidenberg, dated May 27, 1998, and submitted with the "Reply to Office Action" dated May 12, 2005). Under the circumstances, the Examiner's position that (-)-gossypol would be readily predicted to have an appropriate efficacy profile to treat cancer in a human based on the teachings in the prior art is not supported by the prior art.

For the foregoing reasons, Appellants respectfully request the reversal of the rejections of the subject patent application.

Respectfully submitted,

/John Kilyk, Jr./

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